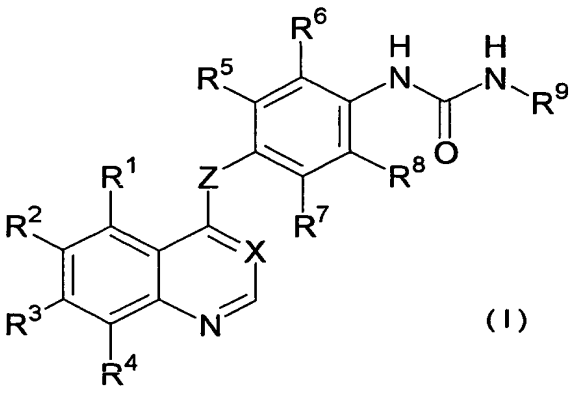
CLAIMS

1. A pharmaceutical composition for use in the treatment or prevention of diseases where the inhibition of autophosphorylation of FMS-like tyrosine kinase 3 (Flt3) and/or its somatic cell variant (Flt3-ITD) is therapeutically or prophylactically effective, which comprises a compound represented by formula (I) or a pharmaceutically acceptable salt or solvate thereof:



(I)

wherein

X represents CH or N,

Z represents O or S,

R^1, R^2, and R^3, which may be the same or different, represent

a hydrogen atom,

hydroxyl,

a halogen atom,

nitro,

cyano,

amino,

C_{1-6} alkyl,

C_{2-6} alkenyl,

C_{2-6} alkynyl,

C_{1-6} alkoxy,

$-(C=O)OR^c$ wherein R^c represents a hydrogen atom or C_{1-4} alkyl, or

$-(C=O)NR^dR^e$ wherein R^d and R^e, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl,

the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} alkoxy groups, which may be represented by R^1, R^2, and R^3, are optionally substituted by hydroxyl; a halogen atom; C_{1-6} alkoxy; C_{1-6} alkylcarbonyl; carboxyl; C_{1-6} alkoxycarbonyl; -(C=O)-$NR^{10}R^{11}$ wherein R^{10} and R^{11}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{10} and R^{11} may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C_{1-6} alkyl or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C_{1-6} alkyl group is further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group; or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group in which the carbocyclic or heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, a halogen atom, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl groups are further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and, when the carbocyclic or heterocyclic group is substituted by two C_{1-6} alkyl groups, the two alkyl groups may combine together to form an alkylene chain, or the carbocyclic or heterocyclic group may be a bicyclic group condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic group;

one or two hydrogen atoms on the amino group, which may be represented by R^1, R^2, and R^3, are optionally substituted by C_{1-6} alkyl which is further optionally substituted by hydroxyl or C_{1-6} alkoxy;

R^4 represents a hydrogen atom;

all of R^5, R^6, R^7, and R^8 represent a hydrogen atom, or any one or two of R^5, R^6, R^7, and R^8 represent a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, amino, or hydroxyl with all the remaining groups representing a hydrogen atom, and

R^9 represents C_{1-4} alkyl substituted by a substituent selected from the group consisting of a saturated three- to nine-membered

carbocyclic group optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl; i-propyl optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl; t-butyl optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl; C_{1-4} alkoxy; and $-NR^aR^b$ wherein R^a and R^b, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^a and R^b may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group, or R^9 represents a saturated three- to nine-membered carbocyclic group optionally substituted by one to three C_{1-4} alkyl groups.

2. The pharmaceutical composition according to claim 1, wherein the disease where the inhibition of autophosphorylation of Flt3 and/or Flt3-ITD is therapeutically or prophylactically effective is hematopoietic malignancy.

3. The pharmaceutical composition according to claim 2, wherein the hematopoietic malignancy is acute myelocytic leukemia or myelodysplastic syndrome.

4. The pharmaceutical composition according to claim 1, wherein the disease where the inhibition of autophosphorylation of Flt3 and/or Flt3-ITD is therapeutically or prophylactically effective is an immunological disease caused by abnormal proliferation of B cells, dendritic cells, or natural killer cells.

5. The pharmaceutical composition according to claim 1, which is used in the treatment or prevention of diseases where the inhibition of autophosphorylation of Flt3 is therapeutically or prophylactically effective.

6. The pharmaceutical composition according to claim 5, wherein the disease where the inhibition of autophosphorylation of Flt3 is therapeutically or prophylactically effective is hematopoietic malignancy.

7. The pharmaceutical composition according to claim 6, wherein the hematopoietic malignancy is acute myelocytic leukemia or myelodysplastic syndrome.

8. The pharmaceutical composition according to claim 5, wherein the disease where the inhibition of autophosphorylation of Flt3 is therapeutically or prophylactically effective is an immunological disease caused by abnormal proliferation of B cells, dendritic cells, or natural killer cells.

9. The pharmaceutical composition according to claim 1, which is

used in the treatment or prevention of diseases where the inhibition of autophosphorylation of Flt3-ITD is therapeutically or prophylactically effective.

10. The pharmaceutical composition according to claim 9, wherein the disease where the inhibition of autophosphorylation of Flt3-ITD is therapeutically or prophylactically effective is hematopoietic malignancy.

11. The pharmaceutical composition according to claim 10, wherein the hematopoietic malignancy is acute myelocytic leukemia or myelodysplastic syndrome.

12. The pharmaceutical composition according to claim 9, wherein the disease where the inhibition of autophosphorylation of Flt3-ITD is therapeutically or prophylactically effective is an immunological disease caused by abnormal proliferation of B cells, dendritic cells, or natural killer cells.

13. The pharmaceutical composition according to any one of claims 1 to 12, wherein X represents CH and Z represents O.

14. The pharmaceutical composition according to any one of claims 1 to 13, wherein R^1 represents a hydrogen atom and R^2 and R^3, which may be the same or different, represent optionally substituted C_{1-6} alkoxy.

15. The pharmaceutical composition according to any one of claims 1 to 14, wherein R^1 represents a hydrogen atom, R^2 and R^3, which may be the same or different, represent -O-(CH_2)p-R^{12} wherein p is an integer of 0 to 6, -(CH_2)p- is optionally substituted by C_{1-6} alkyl, hydroxyl, or a halogen atom, and R^{12} represents a hydrogen atom; hydroxyl; a halogen atom; C_{1-6} alkoxy; C_{1-6} alkylcarbonyl; carboxyl; C_{1-6} alkoxycarbonyl; -(C=O)-$NR^{13}R^{14}$ wherein R^{13} and R^{14}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{13} and R^{14} may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C_{1-6} alkyl or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C_{1-6} alkyl group is further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered

carbocyclic or heterocyclic group; or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group in which the carbocyclic or heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl groups are further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and, when the carbocyclic or heterocyclic group is substituted by two C_{1-6} alkyl groups, the two alkyl groups may combine together to form an alkylene chain, or the carbocyclic or heterocyclic group may be a bicyclic group condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic ring.

16. The pharmaceutical composition according to any one of claims 1 to 15, wherein all of R^5, R^6, R^7, and R^8 represent a hydrogen atom; or R^6 represents a fluorine atom, and R^5, R^7, and R^8 represent a hydrogen atom; or R^5 represents a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, or amino, and R^6, R^7, and R^8 represent a hydrogen atom; or R^5 and R^7 represent a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, or amino, and R^6 and R^8 represent a hydrogen atom.

17. The pharmaceutical composition according to any one of claims 1 to 16, wherein R^9 represents $-(CH_2)s-R^{51}$ wherein s is an integer of 1 to 4, and R^{51} represents a saturated three- to seven-membered carbocyclic group; i-propyl optionally substituted by hydroxyl; t-butyl optionally substituted by hydroxyl; C_{1-4} alkoxy; or $-NR^{52}R^{53}$ wherein R^{52} and R^{53}, which may be the same or different, represent a hydrogen atom, or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{52} and R^{53} may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group, or R^9 represents a saturated five- to seven-membered carbocyclic group optionally substituted by one to three C_{1-4} alkyl groups.

18. The pharmaceutical composition according to claim 1, wherein

X represents CH or N,

Z represents O or S,

R^1, R^2, and R^3, which may be the same or different, represent

a hydrogen atom,
hydroxyl,
a halogen atom,
nitro,
amino,
C_{1-6} alkyl,
C_{2-6} alkenyl,
C_{2-6} alkynyl, or
C_{1-6} alkoxy,

the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} alkoxy groups, which may be represented by R^1, R^2, and R^3, are optionally substituted by hydroxyl; a halogen atom; C_{1-6} alkoxy; C_{1-6} alkylcarbonyl; carboxyl; C_{1-6} alkoxycarbonyl; -(C=O)-$NR^{10}R^{11}$ wherein R^{10} and R^{11}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{10} and R^{11} may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C_{1-6} alkyl or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C_{1-6} alkyl group is further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group; or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group in which the carbocyclic or heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl groups are further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and, when the carbocyclic or heterocyclic group is substituted by two C_{1-6} alkyl groups, the two alkyl groups may combine together to form an alkylene chain, or the carbocyclic or heterocyclic group may be a bicyclic group condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic ring;

one or two hydrogen atoms on the amino group, which may be represented by R^1, R^2, and R^3, are optionally substituted by C_{1-6} alkyl

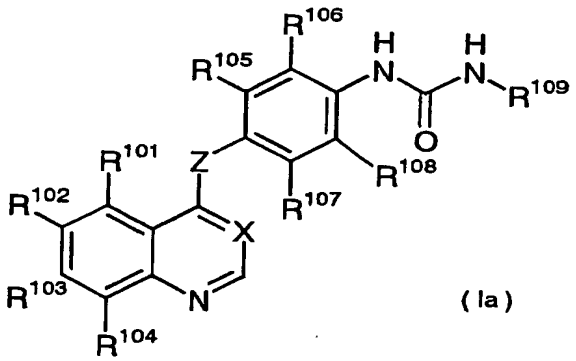
which is further optionally substituted by hydroxyl or C_{1-6} alkoxy;

R^4 represents a hydrogen atom;

all of R^5, R^6, R^7, and R^8 represent a hydrogen atom, or any one or two of R^5, R^6, R^7, and R^8 represent a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, or amino with all the remaining groups representing a hydrogen atom, and

R^9 represents C_{1-4} alkyl substituted by a substituent selected from the group consisting of a saturated three- to seven-membered carbocyclic group; i-propyl optionally substituted by hydroxyl; t-butyl optionally substituted by hydroxyl; C_{1-4} alkoxy; and $-NR^aR^b$ wherein R^a and R^b, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^a and R^b may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group, or R^9 represents a saturated five- to seven-membered carbocyclic group optionally substituted by one to three C_{1-4} alkyl groups.

19. The pharmaceutical composition according to claim 1, wherein said compound represented by formula (I) is represented by formula (Ia):



(Ia)

wherein

X represents CH or N,

Z represents O or S,

R^{101} and R^{104} represent a hydrogen atom,

R^{102} and R^{103}, which may be the same or different, represent a hydrogen atom,

hydroxyl,

a halogen atom,

nitro,

cyano,

$-NR^{111}R^{112}$ wherein R^{111} and R^{112}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl,

$-(C=O)OR^{113}$ wherein R^{113} represents a hydrogen atom or C_{1-4} alkyl,

$-(C=O)NR^{114}R^{115}$ wherein R^{114} and R^{115}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl,

C_{1-6} alkoxy,

C_{1-6} alkyl,

C_{1-6} alkenyl, or

C_{1-6} alkynyl,

the C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl are optionally substituted by hydroxyl; a halogen atom; C_{1-4} alkoxy; $-NR^{116}R^{117}$ wherein R^{116} and R^{117}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl and the alkyl group is further optionally substituted by hydroxyl or C_{1-4} alkoxy; or a saturated or unsaturated three- to eight-membered carbocylic or heterocyclic group in which the cyclic group is optionally substituted by hydroxyl, a halogen atom, C_{1-4} alkyl, or C_{1-4} alkoxy,

all of R^{105}, R^{106}, R^{107}, and R^{108} represent a hydrogen atom, or any one or two of R^{105}, R^{106}, R^{107}, and R^{108} represent hydroxyl, C_{1-4} alkyl, C_{1-4} alkoxy, amino, nitro, or a halogen atom with all the remaining groups representing a hydrogen atom,

R^{109} represents $-(CH_2)n-R^{110}$ wherein n is 2, 3, or 4, and R^{110} represents i-propyl optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl; t-butyl optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl; or a three- to nine-membered saturated carbocyclic group optionally substituted by C_{1-4} alkyl, C_{1-4} alkoxy, or hydroxyl.

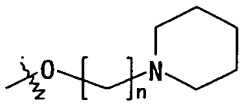
20. The pharmaceutical composition according to claim 19, wherein R^{102} and R^{103}, which may be the same or different, represent C_{1-6} alkoxy and the C_{1-6} alkoxy is optionally substituted by hydroxyl; a halogen atom; C_{1-4} alkoxy; $-NR^{116}R^{117}$ wherein R^{116} and R^{117}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl and the alkyl group is further optionally substituted by hydroxyl or C_{1-4} alkoxy; or

a saturated or unsaturated three- to eight-membered carbocylic or heterocyclic group in which the cyclic group is optionally substituted by hydroxyl, halogen atom, C_{1-4} alkyl, or C_{1-4} alkoxy.

21. The pharmaceutical composition according to claim 20, wherein R^{102} and R^{103}, which may be the same or different, represent C_{1-6} alkoxy in which the alkoxy group is optionally substituted by a saturated or unsaturated three- to eight-membered carbocylic or heterocyclic group and the cyclic group is further optionally substituted by hydroxyl, a halogen atom, C_{1-4} alkyl, or C_{1-4} alkoxy.

22. The pharmaceutical composition according to claim 21, wherein R^{102} and R^{103}, which may be the same or different, represent C_{1-4} alkoxy in which the alkoxy group is optionally substituted by a saturated five- to seven-membered heterocyclic group and the cyclic group is further optionally substituted by C_{1-4} alkyl.

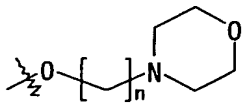
23. The pharmaceutical composition according to claim 22, wherein said substituted C_{1-4} alkoxy group is a group represented by



n=2, 3, 4

24. The pharmaceutical composition according to claim 23, wherein n is 2.

25. The pharmaceutical composition according to claim 22, wherein said substituted C_{1-4} alkoxy group is a group represented by



n=2, 3, 4

26. The pharmaceutical composition according to claim 25, wherein n is 2.

27. The pharmaceutical composition according to any one of claims 19 to 26, wherein one of R^{102} and R^{103} represents unsubstituted C_{1-6} alkoxy and the other represents substituted C_{1-6} alkoxy.

28. The pharmaceutical composition according to claim 27,

wherein R^{102} represents unsubstituted C_{1-6} alkoxy and R^{103} represents substituted C_{1-6} alkoxy.

29. The pharmaceutical composition according to claim 28, wherein R^{102} represents methoxy.

30. The pharmaceutical composition according to any one of claims 19 to 29, wherein X represents CH.

31. The pharmaceutical composition according to any one of claims 19 to 30, wherein Z represents O.

32. The pharmaceutical composition according to any one of claims 19 to 31, wherein all of R^{105}, R^{106}, R^{107}, and R^{108} represent a hydrogen atom, or any one or two of R^{105}, R^{106}, R^{107}, and R^{108} represent C_{1-4} alkyl, C_{1-4} alkoxy, or a halogen atom with all the remaining groups representing a hydrogen atom.

33. The pharmaceutical composition according to claim 32, wherein R^{105} represents methoxy and R^{106}, R^{107}, and R^{108} represent a hydrogen atom.

34. The pharmaceutical composition according to claim 32, wherein R^{105} represents methyl and R^{106}, R^{107}, and R^{108} represent a hydrogen atom.

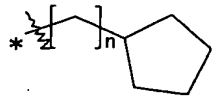
35. The pharmaceutical composition according to claim 32, wherein R^{105} represents a halogen atom and R^{106}, R^{107}, and R^{108} represent a hydrogen atom.

36. The pharmaceutical composition according to claim 35, wherein the halogen atom represents a chlorine or fluorine atom.

37. The pharmaceutical composition according to claim 35, wherein the halogen atom represents a fluorine atom.

38. The pharmaceutical composition according to claim 32, wherein all of R^{105}, R^{106}, R^{107}, and R^{108} represent a hydrogen atom.

39. The pharmaceutical composition according to any one of claims 19 to 38, wherein R^{109} is a group represented by

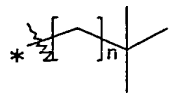


n=2, 3, 4

40. The pharmaceutical composition according to claim 39,

wherein n is 2.

41. The pharmaceutical composition according to any one of claims19 to 38, wherein R^{109} is a group represented by



n=2, 3

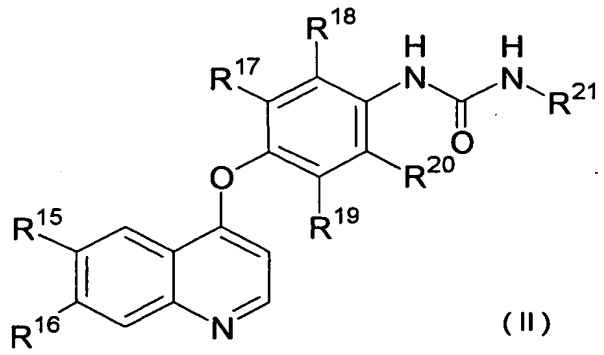
42. The pharmaceutical composition according to claim 41, wherein n is 2.

43. The pharmaceutical composition according to claim 19, wherein the compound represented by formula (Ia) is 1-(3,3-dimethyl-butyl)-3-{3-fluoro-4-[6-methoxy-7-(2-piperidin-1-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-urea.

44. The pharmaceutical composition according to claim 19, wherein the compound represented by formula (Ia) is 1-(2-cyclopentyl-ethyl)-3-{3-fluoro-4-[6-methoxy-7-(2-piperidin-1-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-urea.

45. The pharmaceutical composition according to claim 19, wherein the compound represented by formula (Ia) is 1-(2-cyclopentyl-ethyl)-3-{2-fluoro-4-[6-methoxy-7-(2-piperidin-1-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-urea.

46. The pharmaceutical composition according to claim 1, wherein the compound represented by formula (I) is represented by formula (II):



(II)

wherein

R^{15} and R^{16}, which may be the same or different, represent -O-

$(CH_2)r$-R^{22} wherein r is an integer of 0 to 6, -$(CH_2)r$- is optionally substituted by C_{1-6} alkyl, hydroxyl, or a halogen atom, and R^{22} represents a hydrogen atom; hydroxyl; a halogen atom; C_{1-6} alkoxy; C_{1-6} alkylcarbonyl; carboxyl; C_{1-6} alkoxycarbonyl; -(C=O)-$NR^{23}R^{24}$ wherein R^{23} and R^{24}, which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{23} and R^{24} may combine with a nitrogen atom attached thereto to form a saturated five- or six-membered heterocyclic group; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C_{1-6} alkyl or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C_{1-6} alkyl group is further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group; or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group in which the carbocyclic or heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl groups are further optionally substituted by hydroxyl, C_{1-6} alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and, when the carbocyclic or heterocyclic group is substituted by two C_{1-6} alkyl groups, the two alkyl groups may combine together to form an alkylene chain, or the carbocyclic or heterocyclic group may be a bicyclic group condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic ring,

all of R^{17}, R^{18}, R^{19}, and R^{20} represent a hydrogen atom, or any one or two of R^{17}, R^{18}, R^{19}, and R^{20} represent a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, or amino with all the remaining groups representing a hydrogen atom, and

R^{21} represents -$(CH_2)t$-R^{61} wherein t is an integer of 1 to 4 and R^{61} represents a saturated three- to seven-membered carbocyclic group; i-propyl optionally substituted by hydroxyl; t-butyl optionally substituted by hydroxyl; C_{1-4} alkoxy; or –$NR^{62}R^{63}$ wherein R^{62} and R^{63}, which may be the same or different, represent a hydrogen atom, or C_{1-4} alkyl optionally substituted by hydroxyl, or R^{62} and R^{63} may combine with a nitrogen

atom attached thereto to form a saturated five- or six-membered heterocyclic group, or R^{21} represents a saturated five- to seven-membered carbocyclic group optionally substituted by one to three C_{1-4} alkyl groups.

47. The pharmaceutical composition according to claim 46, wherein R^{15} and R^{16} represent -O-(CH_2)r-H wherein r is an integer of 1 to 4 and the -(CH_2)r- part is unsubstituted, or any one of R^{15} and R^{16} repersents -O-(CH_2)r-H wherein r is an integer of 1 to 4 and the -(CH_2)r- part is unsubstituted with the other representing -O-(CH_2)r-R^{22} wherein r is an integer of 1 to 4, the -(CH_2)r- part is unsubstituted, and R^{22} represents optionally substituted amino or an optionally substituted saturated three- to eight-membered heterocyclic group,

all of R^{17}, R^{18}, R^{19}, and R^{20} represent a hydrogen atom, or any one or two of R^{17}, R^{18}, R^{19}, and R^{20} represent a halogen atom, C_{1-4} alkyl, C_{1-4} alkoxy, nitro, or amino with all the remaining groups representing a hydrogen atom, and

R^{21} represents -(CH_2)t-R^{61}, wherein t is an integer of 1 to 4 and R^{61} represents a saturated five- to seven-membered carbocyclic group; i-propyl; t-butyl optionally substituted by hydroxyl; C_{1-4} alkoxy; or -$NR^{62}R^{63}$ wherein R^{62} and R^{63}, which may be the same or different, represent C_{1-4} alkyl, or R^{21} represents a five- to seven-membered carbocyclic group optionally substituted by 1 to 3 C_{1-4} alkyl groups.

48. The pharmaceutical composition according to claim 46, wherein R^{15} and R^{16} represent -O-(CH_2)r-H wherein r is an integer of 1 to 4 and the -(CH_2)r- part is unsubstituted, or any one of R^{15} and R^{16} represents -O-(CH_2)r-H wherein r is an integer of 1 to 4 and the -(CH_2)r- part is unsubstituted with the other representing -O-(CH_2)r-R^{22} wherein r is an integer of 1 to 4, the -(CH_2)r- part is unsubstituted, and R^{22} represents optionally substituted amino or an optionally substituted saturated three- to eight-membered heterocyclic group,

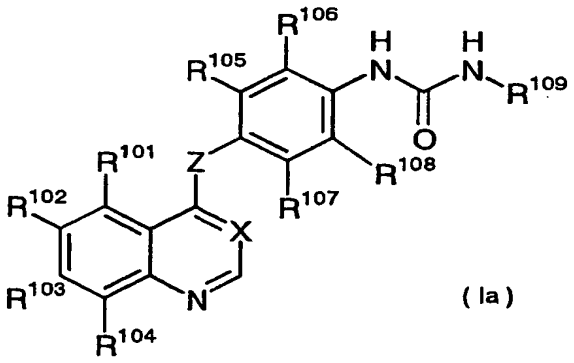
all of R^{17}, R^{18}, R^{19}, and R^{20} represent a hydrogen atom; or R^{18} represents a fluorine atom, and R^{17}, R^{19}, and R^{20} represent a hydrogen atom; or R^{17} represents a halogen atom, C_{1-4} alkyl, or C_{1-4} alkoxy, and R^{18}, R^{19}, and R^{20} represent a hydrogen atom; or R^{17} and R^{19} represent a halogen atom, C_{1-4} alkyl, or C_{1-4} alkoxy, and R^{18} and R^{20} represent a hydrogen atom, and

R^{21} represents $-(CH_2)t-R^{61}$, wherein t is an integer of 2 or 3 and R^{61} represents a saturated five- to seven-membered carbocyclic group or t-butyl, or R^{21} represents a five- to seven-membered carbocyclic group optionally substituted by one to three C_{1-4} alkyl groups.

49. A method for treating or preventing a disease where the inhibition of autophosphorylation of Flt3 and/or Flt3-ITD is therapeutically or prophylactically effective, which comprises the step of administering a compound or a pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 48 together with a pharmaceutically acceptable carrier, to a mammal.

50. Use of a compound or a pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 48, for the manufacture of a medicament used in the treatment or prevention of diseases where the inhibition of autophosphorylation of Flt3 and/or Flt3-ITD is therapeutically or prophylactically effective.

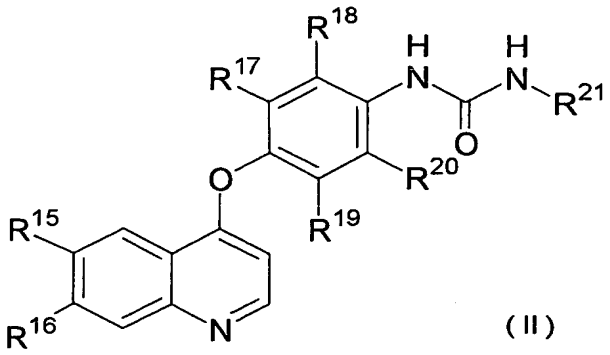
51. A compound represented by formula (Ia) or a pharmaceutically acceptable salt or solvate thereof:



(Ia)

wherein X, Z, R^{101}, R^{102}, R^{103}, R^{104}, R^{105}, R^{106}, R^{107}, R^{108}, and R^{109} are as defined in claim 19.

52. A compound represented by formula (II) or a pharmaceutically acceptable salt or solvate thereof:



(II)

wherein R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, and R^{21} are as defined in claim 46.

53. A pharmaceutical composition comprising a compound according to claim 51 or 52 or a pharmaceutically acceptable salt or solvate thereof.